

Epidemiology Concepts

Some definitions might help some readers better understand epidemiology studies.

Epidemiology is the division of medical science concerned with defining and explaining the inter-relationships of the host, agent and environment in causing disease and, ultimately, death. The purpose of an epidemiology report is to (1) determine if the actual number of deaths are higher or lower than expected and (2) is there a known or suspected reason for the increased (or decreased) number of deaths?

Epidemiology uses the following concepts and language:

First, a definition of a term common in epidemiology – cohort. Normally a “cohort” is a group, especially of warriors or soldiers. Epidemiologists have expanded this definition to include a group of studied persons (usually dead) that are linked together by one or more common characteristics. The size and characteristics of the cohort are controlled by the epidemiologists and a great deal of care is exercised in selecting the “cohort”.

As will be seen in specific studies, Dow seems to use a fair amount of “flexibility” in establishing the cohort, especially in follow-up revisions of prior studies.

Epidemiology reports, if nothing else, are heavy on statistics. The important ones are defined below.

1. Standardized Mortality Ratio (SMR): the actual number of deaths in a time period divided by the expected number of deaths in the same time period. The resulting number is then multiplied by 100. From some reason, epidemiologists do not “count” death, they “observe” death and actual deaths are labeled as “observations”. Another unique concept. Observed deaths should be a simple matter except that most epidemiology reports seem to ignore some actual deaths for a wide variety of reasons. Each report will normally indicate which deaths have been “observed” and which have been ignored and why. You may have to read the fine print, but this information is usually included. A cynic might say that some deaths are excluded to reduce the overall mortality ratio. If a company is carrying out or paying for the study, an overall mortality

ratio of less than 100 is welcomed. A SMR of less than 100 signifies that the observed deaths are less than expected thereby “proving” that the employees being studied are healthier than the national average. Whether this conclusion is “statistically significant” will be discussed in a few paragraphs.

2. “Expected” deaths is also a very simple concept but extremely difficult to calculate and even much harder for a reader to confirm. The basic concept is “how many unexposed persons are expected to die in the same years as the study period.” A large amount of data exists at the national and state level. Most expected deaths for company employees are based on the US white male population. All that is needed is (1) the birthday of each employee being studied and (2) the time period of the study (beginning and ending dates) and the expected death data can be readily obtained from a variety of sources. The number of expected deaths is obtained by multiplying the average death rate (unusually given as the number of deaths per 100,000 population) by the total number of persons (both living and dead) in the cohort. A consistency of data makes a comparison between various mortality studies reasonably easy. Be very leery of any epidemiology study that uses other data bases other than the US population. It is perfectly acceptable to compare expected mortality from the US average population with expected mortality predicted from other sources, such as state or regional information, but the conclusions should be based on the average US population, as adjusted for gender, age, date of birth and the ending date of the study period.

There is a factor in the US population data used to estimate the number of expected deaths that requires additional comment. The US population data is based on the actual deaths of both persons healthy enough to work and those too sick to work. Since industrial studies, such as Dow’s, only examine the mortality of workers that were healthy enough to be hired initially, the SMR of the industrial cohort, for All Causes and, at times, for All Cancers, is generally less than 100. Some companies like to take credit for the lower mortality indicating that the lower death rates are due to improved health benefits and, possibly, a more health life style. While there is a small amount of truth in those claims, the real reason for the lower SMR is that the “expected” deaths include the deaths of those too sick to work.

As the industrial cohort ages, the “age” of the reference US population also increases. The “expected” number of deaths declines with age since those persons too sick to work have died. Very few industrial epidemiology studies explain that the lower overall mortality of the employees is actually a statistical anomaly. One Dow report (see 5. Statistically Insignificant, below) did allude to this.

3. Relative Risk: In order to compare the mortality of exposed workers that were well enough to work with non-exposed workers that were also well enough to work and, to exclude those too sick to work from the calculations, some studies will also include a comparison of the actual deaths being experienced by a hand-picked group of non-exposed workers. Ideally, each hand-picked, non-exposed subject will exactly match the sex, age, birthday pay status and other characteristics of a corresponding member of the exposed cohort. Rather than using the average US population as the non-exposed cohort, the “ideal” relative risk cohort exactly matches the characteristics of the studied cohort, except for a key characteristic, in this case, dioxin exposure. However, the non-exposed relative risk cohort is rarely exactly identical to the exposed cohort.

There are a few problems with the Relative Risk approach. For example, a Relative Risk analysis was included in the 2002 update of four company studies that tracked the mortality of roughly 2,200 Dow workers exposed to dioxins. The RR analysis was based on a Dow study that encompassed 42,076 males that worked in the Midland and Bay City plants. The actual number used in the RR analysis was approximately 28,995 employees. In other words, Dow examined and rejected 13,801 male workers as not being suitable for the RR cohort. The Dow update did not provide a great deal of information on why the 28,995 employees were accepted and why the more than 13,000 employees were rejected. Questions of “selection bias” remain unanswered. A great deal of faith is required to accept the RR analysis. Since the 2002 update contained errors of significance (see review of Brodner, 2002 on the Mortality Studies page), the validity of the RR analysis can not be accepted without further examination.

This is a common problem in any industrial study... a great deal of the epidemiology methodology must be taken on faith.

4. 95% Confidence Interval: Every SMR that is presented in an epidemiology report is usually associated with a range of SMR values that indicates that there is a 95% probability that the actual SMR will be between the ranges given. Generally, if the lower 95% CI is above 100, the SMR is “statistically significant”. A “quality” study will often include a determination of “*p value*” which is a statistic that is used for hypothesis testing. The *p value* is calculated in relationship to a specific hypothesis, usually the *null hypothesis*, which states that there is no relationship between dioxin exposure and each disease category. In many reports, *p values* are not provided. They must exist but, again, faith is required.

5. Statistically Insignificant: A number of Dow reports indicate that, even though the SMR is greater than 100 (more deaths than expected), the increased deaths are statistically “insignificant”. This may or may not be true since proof of the determination is usually not provided. The methodology that was used is generally identified, but never the actual calculations. However, “statistically insignificant” is a two way street. Dow has claimed that the health of its employees is better than the average resident of Michigan or the United States. This claim may be based on numerous studies in which the SMR for the Dow employees for all causes of death is less than 100. In a study of 2,192 Dow employees (1940 – 1982) that were exposed to higher chlorinated dioxins, the report stated, “The SMR for all causes of death was 93. Thus, fewer deaths occurred than expected based on statistics for the corresponding United States white male population but the difference was not statistically significant (95% confidence limits 84 – 104).¹ This was the only Dow study that stated whether the SMR for All Causes was statistically insignificant or not. All of the other Dow studies posted on Dow’s website are silent on this key point.

Perhaps, the Dow assurance should be changed as follows, “Numerous studies – including vital studies conducted by the Environmental Protection Agency (*unidentified*), Midland County Public Health Department and Dow show that the health of Midland County residents and Dow workers is better than state and national averages, *but the improvement is statistically insignificant.*”

¹ Cohort Mortality Study of Chemical Workers With Potential Exposure to the Higher Chlorinated Dioxins, Ott MG, Olson RA, et al, *Journal of Occupational Medicine*, 29-No. 5, May, 1987

6. Dose Response: In some Dow reports, it has been noted that, when a potential association between health effect and dioxin exposure seems to be apparent (even to the non-epidemiologist), Dow will dismiss the association by stating that a dose response relationship has not been found. Basically, the concept is that the observed medical effect must increase with the amount of exposure for an association to be confirmed. Seems like a rather convincing argument.

However, the NIOSH study on employees exposed to TCDD offered this insight which is somewhat different than Dow's. "In addition, a dose response relationship is generally viewed as strong evidence for an association when it is present, but as fairly weak evidence against an association when it is absent."² In other words, the lack of a dose response relationship really doesn't prove anything despite Dow's insistence to the contrary.

I hope that this information will be of help to the readers as the Dow mortality studies are examined in greater detail.

² Cancer Mortality in Workers Exposed to 2,3,7,8-Tetrachlorodibenzo-p-dioxin, Fingerhut MA, Halperin WE, et al, *The New England Journal of Medicine*, Vol. 324 No. 4, Jan 24, 1991